The Absence of Kinetic Stereoselectivity in the Copper(II)–Histidine Catalysed Hydrolysis of Histidine Methyl Ester

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HIX AND JONES[1] have recently described a marked kinetic stereoselective effect in the metal complex-catalysed hydrolysis of histidine methyl ester. The rate of hydrolysis of the L-(+)-ester in the presence of nickel(II)–D-(−)-histidine was 40% greater than in the presence of nickel(II)–L-(+)-histidine. Thus the nickel(II) complex of histidine catalyses the hydrolysis of histidine methyl ester more effectively if the ester and histidine are of opposite configurations. However, our measurements on the analogous copper(II) system show that no kinetic stereoselectivity occurs.

In the 1 : 1 : 1 systems of histidine (A^-), histidine methyl ester (E), and copper(II) the following equilibria occur at pH 9.

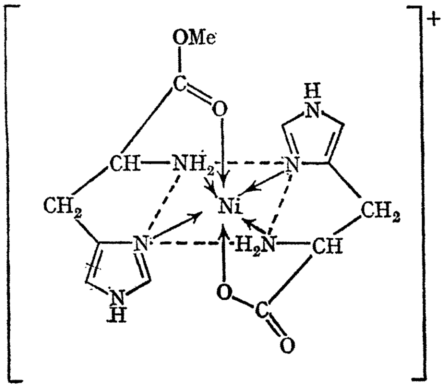
$$Cu^{2+} + E + A^- \rightleftharpoons CuEA^+;\ K_{111} = [CuEA]/[Cu^{2+}][E][A^-]$$

$$Cu^{2+} + 2E \rightleftharpoons CuE_2{}^{2+};\ K^{E}_{12} = [CuE_2{}^{2+}]/[Cu^{2+}][E]^2$$

$$Cu^{2+} + 2A^- \rightleftharpoons CuA_2;\ K^{A}_{12} = [CuA_2]/[Cu^{2+}][A^-]^2$$

The values for the various constants evaluated from potentiometric data at $I = 0{\cdot}1$M and 25°, with the programme

SCOGS[2] are $\log K_{111} = 16{\cdot}93 \pm 0{\cdot}02$, $\log K^{E}_{12} = 14{\cdot}49 \pm 0{\cdot}05$, $\log K^{A}_{12} = 18{\cdot}20 \pm 0{\cdot}02$. At complete neutralisation of the ligand protons (pH >6·7), the percentage of each species can be calculated; % $CuEA^+$ = 66·6, % CuE_2^{2+} = % CuA_2 = 16·7. All potentiometric measurements were made with compounds of the L-series.



(I)

Kinetic measurements were carried out at 25° and I = 0·1M and pH >9, with a pH-stat to monitor the hydrolysis. Plots of the alkali consumption against time for the diastereoisomeric systems of D-(−)-histidine and L-(+)-histidine with L-(+)-histidine methyl ester and copper(II) are essentially superimposable. At constant pH, the reaction is pseudo-first-order in the complexes. A kinetic plot for the data at pH 9·1 for Cu-(L-Hist Me)(D-Hist) is shown in the Figure. Very marked initial curvature is observed, probably due to the initial more rapid base hydrolysis of the species CuE_2^{2+}. As the reaction proceeds the curve becomes linear. This linear portion can probably best be attributed to base hydrolysis of the mixed species $CuEA^+$ Values of k_{obs} have been evaluated from the final linear portions of the curve (Table). We conclude that, within the limits of experimental error, no stereoselectivity occurs in this system.

Similar experiments were carried out with the nickel(II) system, in this case much less initial curvature was observed in the kinetic plots. In agreement with Hix and Jones[1] we find that stereoselectivity does occur with nickel(II), although the stereoselectivity observed by us (33%) is somewhat less than that previously noted (40%) (Table).

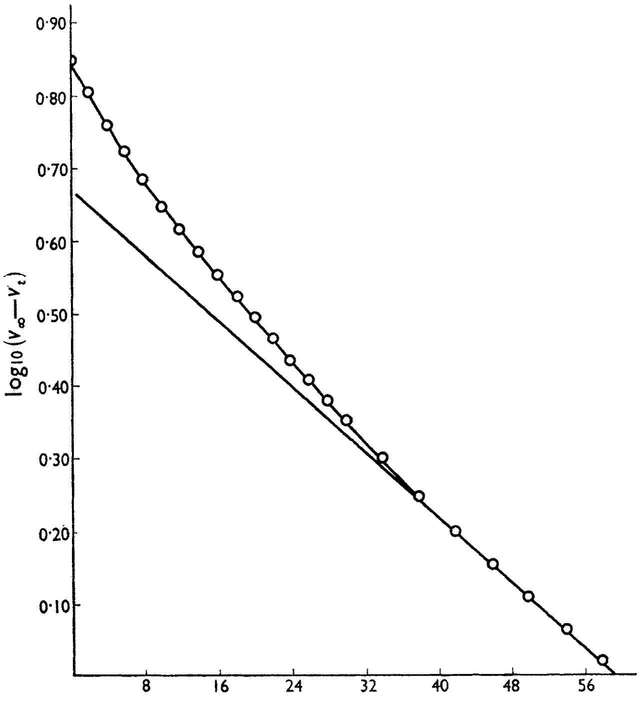
Hix and Jones have attributed the stereoselectivity in the nickel(II) system to a more favourable interaction of the methoxycarbonyl group with the metal ion in one of the six co-ordinate diastereoisomers. It seems probable that the histidine complexes have a *trans*-configuration.[3] With *trans*-D- and -L-mixed ligand complexes there is a possibility of interaction between the carbonyl group of the ester and the metal ion as shown in (I). With *trans*-L and -L-mixed ligand complexes such an interaction should not occur.[4] Copper(II) generally shows a preference for square-planar, or grossly distorted octahedral, structures. With the complex $CuEA^+$ there is probably little, if any, interaction between the methoxycarbonyl group and the copper(II) ion, since the carboxylate group in histidine is a better donor. The complex $CuECl_2$ has recently been isolated[5] and its i.r. spectrum indicates no interaction between the ester grouping and the metal ion. Quite marked differences in behaviour between the two metal-ions may therefore be expected.

TABLE

	pH	$10^2 k_{obs}$ (min.$^{-1}$)	$10^{-3} k_{obs}$/[OH$^-$] (M^{-1} min.$^{-1}$)‡
Cu(L-Hist Me)(D-Hist)$^+$	9·10	2·61	1·59§
Cu(L-Hist Me)(L-Hist)$^+$	9·10	2·87	1·74§
Cu(L-Hist Me)(D-Hist)$^+$	9·30	4·33	1·66§
Cu(L-Hist Me)(L-Hist)$^+$	9·30	4·54	1·74§
Ni(L-Hist Me)(D-Hist)$^+$	9·10	3·34	2·03
Ni(L-Hist Me)(D-Hist)$^+$	9·40	6·42	1·96
Ni(L-Hist Me)(L-Hist)$^+$	9·10	2·51	1·53
Ni(L-Hist Me)(L-Hist)$^+$	9·40	4·85	1·48

‡ At 25° and I = 0·1M. Values of [OH$^-$] calculated from the pH = log {H$^+$} with a value of $y_1 = 0{\cdot}7715$ and $pK_w = 13{\cdot}9965$.

§ These values may be compared with our estimate of $k_{CuEA^+} = 2{\cdot}56 \times 10^{-3}$ M^{-1} min.$^{-1}$ obtained by using the time-ratio method (R. W. Hay and P. J. Morris, *Chem. Comm.*, 1967, 23).



FIGURE

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[1] J. E. Hix and M. M. Jones, *J. Amer. Chem. Soc.*, 1968, **90**, 1723.

[2] I. G. Sayce, *Talanta*, 1968, in the press.

[3] C. C. McDonald and W. D. Phillips (*J. Amer. Chem. Soc.*, 1963, **85**, 3736) have shown for example that in the cobalt(II) complex of histidine a *trans*-arrangement of nitrogen donors occurs.

[4] R. D. Gillard, *Inorg. Chim. Acta Rev.*, 1967, **1**, 69.

[5] R. W. Hay and L. J. Porter, *Austral. J. Chem.*, 1967, **20**, 675.